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Title: Investigating the Immediate and Cumulative Effects of Isometric Squat Exercise for Different Weight Loads on Intraocular Pressure: A Pilot Study

Running head: IOP behavior during isometric squat exercise

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46 **Abstract**

47 **Background:** The execution of resistance exercise against heavy loads promotes an acute
48 intraocular pressure (IOP) rise, which has detrimental effects on ocular health. However, the
49 effect of load on the IOP behaviour during exercise remains unknown due to technical
50 limitations.

51 **Hypothesis:** The IOP monitoring during isometric squat exercise would permit to assess the
52 IOP behaviour during physical effort, and the use of greater loads would induce a higher IOP
53 rise.

54 **Study design:** Randomized cross-sectional study.

55 **Level of evidence:** Level 2.

56 **Methods:** Twenty-six young adults (13 women) performed an isometric squat exercise against
57 three loads relative to their maximum capacity (low, medium and high). IOP was measured
58 before, during (one measurement every six seconds) and after exercise (ten seconds of
59 recovery).

60 **Results:** There was a progressive IOP rise during exercise ($BF_{10}>100$, coefficients of
61 determination for the three loads ranged between 0.90 and 0.95), which was dependent on the
62 load applied ($BF_{10}>100$). Higher IOP values were found in the high load condition in
63 comparison to the medium ($BF_{10}>100$, effect size [ES]=0.63) and low conditions ($BF_{10}>100$,
64 ES=1.41), as well as when the medium load was compared with the low load condition
65 ($BF_{10}>100$, ES=0.67). Men reached higher IOP values in comparison to women during the last
66 measurements in the high load condition. Ten seconds of recovery were enough to obtain IOP
67 values similar to baseline levels ($BF_{10}=0.32$, ES=0.24).

68 **Conclusion:** Isometric squat exercise induces an immediate and cumulative IOP elevation,
69 which is positively associated with the load applied. These IOP increments return to baseline

values after ten seconds of recovery, and men demonstrate a more accentuated IOP rise in comparison to women when high levels of effort are accumulated.

Clinical Relevance: These findings may help to a better management of different ocular conditions, and highlight the importance of an individualized exercise prescription in clinical populations.

Keywords: ocular health; eye care; glaucoma management; rebound tonometry; exercise prescription.

Introduction

It is well known that performing physical exercise on a regular basis promotes a number of beneficial physiological adaptations, which are highly dependent on the type of exercise and subjects' characteristics.⁹ In the field of ophthalmology and optometry, the influence of physical effort on the ocular physiology has been investigated due to its potentially beneficial or harmful effects on eye health.³⁶ One of the ocular indices that has received significant research attention is intraocular pressure (IOP), since it is the only proven modifiable risk factor in the management of glaucoma.¹¹ Managing glaucoma is of critical importance as it is one leading cause of irreversible blindness worldwide, and projections of glaucoma prevalence estimate that 76 million of people will suffer from glaucoma in 2020.²⁷ Therefore, identifying the most pertinent interventions, including physical exercise to properly manage glaucoma are of great importance.³⁷

Several factors are known to influence the IOP response to physical exercise, such as the type of physical exercise, participant's fitness level, and exercise intensity, among others.^{31,36,37} Within these factors, the type of physical exercise is probably the factor that has received the most research attention. The majority of studies conclude that low-intensity aerobic exercise or endurance exercise performed against low relative loads reduce IOP in both the short and long-term when IOP is assessed after exercise,^{20,29} whereas the execution of strength exercise with high relative loads is associated with an acute IOP increase.^{26,28,30,31,33} Taken together, these studies recommend avoiding the execution of strength exercises against heavy loads, especially in glaucoma patients or those at risk, and thus, an individualized exercise prescription is recommended for the appropriate management of ocular health.

Due to methodological limitations, IOP behaviour while performing strength exercises remains largely unknown. Regarding strength exercises, the majority of studies have used a pre/post design (i.e., IOP was assessed before and after exercise).^{26,28,33} However, since there is evidence that IOP values change quickly once the strength exercise has ceased,^{20,25,28} it is

essential to continuously assess IOP behaviour while performing strength exercises. Notably, isometric exercises where athletes maintain the same body position during the entire set, allowed exploration of IOP variations during different modalities of this exercise.^{1,3} For example, Bakke et al., (2009)¹ investigated IOP variations by employing an electronic continuous-indentation tonometer while participants executed a 2-minute handgrip isometric exercise (40% maximal voluntary contraction of the forearm), whereas Castejon et al., (2010)³ explored IOP behaviour with a Goldman tonometer every 30 seconds during a 2-min handgrip (30% of maximal voluntary contraction) and squat (knees flexed at 90° without any additional load) isometric exercises. These investigations provide evidence that isometric exercises induce a progressive IOP rise, in particular higher increments in the squat exercise compared to the handgrip exercise. Nevertheless, no study has continuously determined IOP behaviour during the execution of isometric exercises performed against different loading magnitudes, as it has been carried out with dynamic strength exercises in a pre/post design.^{28,31}

To address this research caveat in related literature, the main objectives of the present study were: (1) to evaluate IOP behaviour during a 1-min isometric squat exercise with semi-continuous IOP assessment, and (2) to determine the impact of the load applied on IOP measurements. Complementarily, (3) we tested possible differences in IOP changes between men and women. We hypothesized that (1) IOP measurements would progressively increase during a 1-min exercise period,^{1,3} (2) a significant IOP rise will be induced while executing strength efforts; a greater IOP rise is expected for higher relative loads, as shown with dynamic strength exercises.²⁸ Finally, the lack of similar studies together with previous findings reporting that the between-sex differences in the physiological responses to isometric exercise are dependent on the variable assessed,^{15,35} (3) the null hypothesis is that no differences in IOP variations will be observed between men and women.

Methods

Participants

An a-priori power analysis to determine the sample size, assuming an effect size of 0.20, alpha of 0.05 and power of 0.90, predicted a required sample size of 24 participants (12 per group) using mixed ANOVA. At this point, twenty-six physically active university students took part in this study (13 men, mean \pm standard deviation [SD]; [age: 23.4 ± 2.8 years] and 13 women [age: 22.1 ± 2.5 years]). Participants were free of any physical limitation that could compromise tested performance and had no history of any ocular or cardiovascular disease or surgery. Participants were instructed to avoid any strenuous exercise two days prior to each testing session. All participants had 2 or more years of experience in strength training. Participants were first informed of the procedures involved and then signed a written informed consent form prior to initiating the study. The study protocol adhered to The Code of Ethics of the World Medical Association and was approved by the Institutional Review Board.

Experimental design and procedure

A mixed design was used to evaluate the influence of isometric squat exercise performed against different loads on IOP values in men and women. IOP measurements were taken before and after the exercise as well as during the 1-min isometric exercise by semi-continuous IOP assessment. The within-participants factors were the load (low, medium, high) and the point of measure (before exercise, during exercise [points: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10], and recovery), and the sex (men and women) was the between-participants factor. IOP was the dependent variable.

Participants attended to the laboratory on only one occasion. When they arrived to the laboratory, they were read and signed the consent form, and filled-in the demographic questionnaire. Then, participants were instructed to warm-up, and we described how to execute the isometric squat exercise correctly. At this point, an experienced strength and conditioning researcher individually determined the heaviest load that each participant could hold for 1 min during the isometric squat exercise performed at a knee angle of 90° (see below). Following this, participants rested for 10 min before the beginning of the first experimental condition. Participants randomly performed the isometric squat exercise against three different loads that

were separated by 10 min. First, we conducted a baseline measure of IOP, and then participants adopted the squatting position while holding the corresponding load, and an experienced optometrist measured the IOP during the 1 min period (see detail below). When the isometric squat exercise ended, another IOP measurement was obtained after 10 seconds of passive recovery in standing position.

Squat isometric exercise

Participants performed the isometric squat exercise with their feet approximately shoulder-width apart and at a knee angle of 90°. Participants were instructed to hold the static position at 90° knee flexion for 1 min against 3 different loads, which were applied in a randomised order. The minimum loading condition represented the participant's own body mass (i.e., no external load was applied). The maximum loading condition represented the heaviest load with which the participants could hold the isometric squat position for 1 min (45.9 ± 6.5 kg in men and 30.1 ± 5.1 kg in women). The medium loading condition represented a half of the maximum load (26.2 ± 3.3 kg in men and 18.2 ± 2.2 kg in women). The external load for the medium and maximum loading conditions was applied by means of the barbell of a Smith machine (Technogym, Barcelona, Spain) positioned across the top of the shoulders and upper back. A rest period of 10 min was imposed between successive sets. Participants were instructed to avoid the Valsalva maneuver, which has showed to increase IOP during maximal exertion, in absence of other factors.²

Intraocular pressure assessment

A rebound tonometer was used to assess IOP (Icare, TiolatOy, INC. Helsinki, Finland), which has been previously clinically validated²¹ and employed in related research.^{26,32} This apparatus presents some advantages in comparison to others techniques (e.g., Goldman applanation tonometry): (i) it is portable and hand-held, (ii) it can rapidly measure IOP, (iii) the procedure is well-tolerated and (iv) measuring does not require the use of topical anaesthesia.²¹ The inherent characteristics of the tonometer and the exercise (static exercise with neutral neck

position) allowed us to semi-continuously measure IOP. This constitutes the main novelty of this study in comparison to previous investigations, where the effects of different types of strength or endurance exercises were tested in a simple pre/post design.^{26,28,31–33} While exercising, participants were instructed to fixate on a distant target as consecutive measurements were taken against the central cornea. Every six measurements, the mean value is displayed, and the examiner vocalized the IOP value to a research assistant for data logging. During the one-minute isometric exercise, the examiner acquired tens of IOP values in a continuous fashion. Due to (i) the tonometer's inability to acquire IOP measurements at exact time intervals, (ii) the lack of exact timestamps for the measurements and (iii) the manual logging of the values, we describe a process to overcome these technical restrictions and obtain a set of equally distributed values at regular intervals with exact timestamps in the data processing subsection. In addition, a baseline IOP was measured before each exercise, and a recovery measurement was obtained ten seconds following the exercise. All measurements were taken in the right eye.

Data processing

We developed a procedure to obtain a set of equally distributed IOP measurements at regular intervals, thus overcoming the timestamping and lack of automatic logging restrictions of the rebound tonometer, described in the previous section. We based our method on multi-rate digital signal processing, in particular sample-rate conversion which is the process of changing the sampling rate of a discrete sampled signal to obtain a new discrete representation of the underlying continuous signal, in this case the IOP signal.⁸ IOP is a continuous function, as when IOP values rise and fall between two pressures, IOP will always take all intermediate values between those two pressures. In our process we treated the obtained samples as geometric points and create the necessary new points by polynomially interpolating those values, essentially approximating the source, continuous IOP signal, and then re-sampling at 10 discrete intervals for the 1-minute period, i.e., every 6 seconds.

Simply stated, when measuring IOP using the rebound tonometer, we essentially sampled the continuous IOP function at slightly irregular intervals. The obtained values are the values of the IOP function at those moments-in-time. But because the function is continuous we can reconstruct the IOP function from the sample measurements and then re-sample the function at specific, regular intervals, thus obtaining a fixed set of values at these exact intervals. The new data points are estimated within the range of the discrete set of sampled data points.

Statistical analysis

We used a Bayesian approach to test the influence of isometric squat exercise performed against different external loads on IOP. This method of statistical inference presents numerous advantages in comparison to classical “frequentist” approaches.^{19,34} The interpretation of the Bayes Factor (BF) enables the quantification of the evidence for one hypothesis relative to another (alternative vs. null hypotheses), allowing us to determine whether non-significant results confirm the null hypothesis, or whether data are just not sensitive enough to accept any hypotheses. Based on the evidence categories for BF_{10} (alternative against null hypotheses) proposed by Jeffreys (1961)¹³, a BF_{10} higher than 3 reveals substantial evidence for the alternative hypothesis, whereas a BF_{10} lower than 1/3 determinates substantial evidence for the null hypothesis. However a BF_{10} between 1/3 and 3 is considered non-sensitive for accepting any hypothesis (see Table 1 of Wetzels et al. (2011)³⁴ for a detailed description of BF categories).

First, in order to test hypothesis 1, we used a mixed Bayesian ANOVA to evaluate the cumulative effect of a 1-minute isometric squat exercise on IOP, with the load (low, medium, high) and the point of measure (1, 2, 3, 4, 5, 6, 7, 8, 9, and 10) as the within-participants factors, and with sex (men and women) as the between-participants factor. Complementarily, we calculated three separate linear regression analyses to assess the IOP behaviour during the 1-minute isometric effort against each load. To examine the acute impact of the load on IOP (objective 2), we conducted a repeated measures Bayesian ANOVA with the load (low,

medium, high) and the point of measure (before exercise, during effort [average IOP value from the 10 measurements taken during the 1-minute exercise] and after 10 seconds of passive recovery) as the within-participants factor. We also reported Cohen's effect sizes (ES) as they can provide additional evidence of how much the results deviate from the null hypothesis, and they were interpreted as negligible (<0.2), small ($0.2-0.5$), moderate ($0.5-0.8$), and large (≥ 0.8).⁶ The JASP statistics package (version 0.9) was used for statistical analysis.

Results

Aiming to ensure that there were no differences from the baseline IOP values before any of the three exercises, we performed a one-way Bayesian ANOVA with the load (low, medium, high), as the only within-participants factor. We found that there was substantial evidence for the null hypothesis when the three IOP measurements before effort were analysed ($BF_{10}=0.203$), and thus, the baseline IOP values between exercises were similar.

The first set of analysis to assess IOP behaviour during the 1-min isometric squat exercise (objective 1) revealed a decisive evidence for the alternative hypothesis for the load, the point of measure and the interaction load x point of measure ($BF_{10}>100$ in the three cases). This means that significant differences (acceptance of the alternative hypothesis) were found for these factors. Post-hoc comparisons for the different loads demonstrated substantial evidence for the alternative hypothesis between the low and high loads ($BF_{10}>100$, $ES=1.41$), the low and medium loads ($BF_{10}>100$, $ES=0.67$), as well as between the medium and high loads ($BF_{10}>100$, $ES=0.63$). This means that higher IOP values were obtained when the isometric effort was performed against greater loads. The IOP behaviour during the 1-minute isometric squat exercise showed a linear increase over time, with a coefficient of determination (R^2) of 0.91 for the low-load, 0.90 for the medium-load and 0.95 for the high-load (**Figure 1**). Regarding sex, our data were not sensitive enough for the main effect of sex ($BF_{10}=0.586$), whereas the interactions sex x load and sex x point of measure demonstrated substantial evidence to accept the alternative hypothesis ($BF_{10}>100$ in both cases). **Figure 2** displays all the post-hoc

comparisons carried out for all the points of measure and loads, demonstrating that men reached higher IOP values in comparison to women during the last measurements conducted with the high-load condition.

Second, we analysed the impact of the load applied on IOP variations (objective 2); the load factor showed substantial evidence for the null hypothesis ($BF_{10}=0.288$), whereas decisive evidence for the alternative hypothesis was found for the point of measure and the interaction load x point of measure ($BF_{10}>100$ in both cases). This mean that IOP values were considerably different between the three points of measure (baseline, during effort, and during recovery), although, the load did not have a significant impact on IOP behaviour in this case. Post-hoc comparisons for the different loads demonstrated substantial evidence for the alternative hypothesis between the low and high loads ($BF_{10}=9.403$, $ES=0.51$), whereas the comparison between the medium and high loads provided anecdotal evidence for the alternative hypothesis ($BF_{10}=2.062$, $ES=0.37$), and lastly, when the low and medium loads were compared, we found substantial evidence for the null hypothesis ($BF_{10}=0.167$, $ES=0.12$). Regarding the point of measure, there was decisive evidence for the alternative hypothesis in the comparison of the IOP value obtained before effort, and the average value from those taken during isometric effort ($BF_{10}>100$, $ES=2.24$). Similarly, decisive evidence for the alternative hypothesis was found when the average IOP obtained during effort was compared to the recovery IOP measurement ($BF_{10}>100$, $ES=2.12$). Hence, higher IOP values were found for the high load in comparison to the low load, as well as when the IOP values obtained during effort were compared with those taken before effort and during recovery. However, substantial evidence for the null hypothesis was revealed for the comparison between the baseline and recovery IOP values ($BF_{10}=0.32$, $ES=0.24$) (**Figure 3**), suggesting that baseline and recovery IOP values were comparable.

Discussion

The main finding of the present study revealed that IOP linearly increases over time during a 1-min isometric squat exercise. In addition, the application of higher loads was also associated with larger IOP increments, while trivial differences in IOP behaviour were observed between

men and women. These results are in line with previous studies that showed an IOP rise during isometric exercises;^{1,3} however, the present study shows that load is an important modulator of IOP behaviour during isometric effort. Relevantly, although IOP measurements were meaningfully incremented at the end of the 1-min effort (by 4 to 8 mmHg), IOP returned to baseline levels after only 10 seconds of recovery, which evidences the transient nature of IOP changes caused by physical effort, once the effort has ceased. Taken together, these findings highlight that isometric strength exercises, especially when performed against heavy loads, should be avoided when low and stable IOP values are desirable. These findings may have important implications not only for glaucoma patients, but also for the management of other ocular conditions such as myopic fundus pathology or keratoconus where abrupt IOP elevations may provoke stretching of the fundus or cone progression, respectively.¹⁷

Regardless of the load imposed, our data indicate that the time under tension provokes a strong linear IOP rise (R^2 : 0.90-0.95). This linear tendency of IOP values to increase over time agrees with recent evidence on the influence of the accumulated level of effort during resistance training on the structural and neuromuscular adaptations induced by the progressive accumulation of fatigue.²² Similar results have been published by Bakke et al. (2009)¹ who found a linear IOP increase during the handgrip isometric exercise while participants exerted a 40% of the maximal voluntary isometric force, or Castejon et al. (2010)³ who also showed a linear IOP rise, as measured every 30 seconds during a 2-minute period, while the subjects adopted the squatting position without the application of any additional load. Here, we found that the accumulated effect of isometric exercise on IOP is independent of the exercise intensity, and excitingly, the semi-continuous IOP assessment of our study indicates that these effects are essentially instantaneous.

The magnitude of the load applied during the isometric squat exercise significantly influenced IOP variations, being IOP values further increased under higher loading conditions. The average IOP increment during the 1-min isometric squat exercise was 24% for the low load, 37% for the medium load, and 41% for the high load, whereas after 1 min of exercise (i.e., last

point of measure during effort) the IOP was incremented by 36%, 52% and 59% for the low, medium and high loads, respectively. These findings present preliminary evidence with respect to the role of intensity when performing isometric exercises, which are of special relevance since external loads are commonly applied during isometric training.¹⁶ Our data converge with the results found for blood pressure, which have shown that blood pressure increases as a consequence of executing isometric exercises in an intensity-dependent manner.¹⁰ In line with these results, during dynamic strength exercises IOP measurements were positively and linearly correlated with the magnitude of the load applied.^{28,32} Nevertheless, the IOP rises obtained in this study were substantially higher to those found when performing dynamic strength exercises. Based on present outcomes, it is reasonable to recommend abstaining from isometric exercise when maintaining stable IOP levels is desired or necessary, since a higher short-term IOP fluctuation (within a daily IOP curve) has been identified as a considerable risk factor for glaucoma onset and progression.^{7,18}

We only found a significant difference in IOP measurements between men and women when the high-load was applied, with women showing a more stable IOP behaviour during the last two measurements (see figure 2). This result is preliminary, since to the best of our knowledge, no previous study has compared IOP variations during isometric exercise between men and women. These results are in line with accumulated evidence of sex-related differences in the cardiovascular and autonomic regulation,²³ with women exhibiting lower reactivity in comparison to men. In this regard, Wong et al. (2007)³⁵ found a smaller cardiovascular response to isometric exercise in women related to their greater suppression of the dorsal anterior cingulate cortex activity, which has been linked with sympathetic control of the cardiovascular system. Hence, a similar mechanism to the lower physiological reactivity and stronger sympathetic control of the cardiovascular system in women may explain the reduced IOP reactivity observed in women in this study.

Our results revealed that IOP values returned to baseline levels following 10 seconds of passive recovery in all the tested conditions. This finding corroborates that IOP changes

induced by isometric exercise are very transient,¹ which, consequently, has two important implications: (1) the side effects of isometric exercise on the ocular health may only occur during physical effort, and therefore (2) the assessment of IOP variations to different exercises in a pre/post design should be cautiously interpreted, since the post measurements may not reflect the actual IOP variation induced by the corresponding exercise.

There are some factors that may limit the generalizability of these findings, and they should be acknowledged. First, the present results are of special interest for the management of different ocular conditions, however, our experimental sample was formed by young healthy individuals. The inclusion of glaucoma patients, who demonstrably have an altered autoregulatory control of the ocular hemo- and aqueous humour- dynamics and suffer higher IOP fluctuations to a variety of stress tests,⁵ is warranted in future studies. Of note, De Moraes et al. (2018)¹⁸ recently showed that even these transient IOP spikes during the day (when measured with a contact lens sensor) have a detrimental effect on the visual fields of glaucoma patients. Second, previous investigations have stated that fitness level is an important modulator of the IOP response to dynamic strength exercise,³¹ with trained individuals showing a smaller IOP change than untrained counterparts. Therefore, it is recommended that future studies evaluate the mediating role of fitness level on IOP variations in isometric exercise. Third, in our study we continuously evaluated IOP behaviour during a 1-min isometric squat exercise, obtaining an abrupt IOP rise, but it is desirable to continuously monitor IOP behaviour after exercise as well, in order to test IOP recovery following isometric exercise. Fourth, the execution of the Valsalva maneuver provokes IOP fluctuation,² and although participants were asked to avoid it, we cannot discard that they did it unintentionally. Fifth, postural changes are known to alter the ocular hemodynamics,^{12,24} here, all exercises were performed in standing position, and thus, we consider of interest to study the possible influence of adopting different head and body positions on the eye physiology while performing isometric exercises (e.g., abdominal planks). Sixth, ocular physiology is known to be dependent on age and ethnicity and, thus, future studies should consider others age and ethnics groups.⁴ Continuous technological

advancements in ocular imaging techniques (e.g., optical coherence tomography angiography or anterior segment optical coherence tomography) may be incorporated into this line of research in order to further deepen our understanding of ocular physiological responses (e.g., optic nerve integrity and function, retinal oxygenation, aqueous humour drainage, etc.) caused by exercise, aiming to develop the recommendations for exercise prescription in patients with different ocular conditions.¹⁴

In summary, isometric squat exercise provokes a rapid and progressive IOP elevation, and these IOP variations are positively associated with the magnitude of the external load applied during exercise. IOP drops shortly after ceasing the physical effort (10 seconds of recovery), and men exhibited a more accentuated IOP rise at the end of the exercise compared to women. These findings may contribute to establish the most appropriate guidelines for exercise prescription in terms of ocular health, particularly relevant for glaucoma patients or those at high risk of glaucoma. Based on the current findings, we recommend abstaining from isometric squat exercise, particularly under heavy loading conditions, when stable IOP levels are desirable. We encourage future studies to evaluate these effects in clinical populations and to incorporate the most recent developments in ocular imaging techniques in their experimental designs.

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Figure captions

Figure 1. Effects of performing 1-min isometric squat exercise against three different loads on intraocular pressure. The recovery value was taken 10 seconds after exercise, and the grey area represents the 1-minute isometric physical effort. Error bars show the Standard Error. All values are calculated across participants ($n = 26$). Rec = recovery.

Figure 2. Standardized differences (Cohen's d effect size) in the intraocular pressure changes between men and women when performing the isometric squat exercise against three different loads. All values are calculated across participants ($n = 26$). Rec = recovery.

Figure 3. Effects of performing 1-min isometric squat exercise against three different loads on intraocular pressure. The effort value depicts the average IOP from the ten IOP measurements taken during exercise. # and * indicate statistically significant differences between the different points of measure and loads, respectively (corrected p -value < 0.05). Error bars show the Standard Error. All values are calculated across participants ($n = 26$).